

## Ameloblastic Carcinoma

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**Abstract** Ameloblastic carcinoma (AC) is a rare aggressive malignant epithelial odontogenic tumor of the maxillofacial skeleton with a distinct predilection in the mandible. It may appear de novo or originate from a pre-existing ameloblastoma or odontogenic cyst. It exhibits cytological features of ameloblastoma and carcinoma. It may present as a cystic lesion with benign clinical features or as a large tissue mass with ulceration, significant bone resorption and tooth mobility. The clinical course of ameloblastic carcinoma is typically aggressive, with extensive local destruction. Direct extension of the tumour, lymph node involvement and metastasis to various sites has been reported. Wide local excision is the treatment of choice. Regional lymph node dissection should be considered and performed selectively. Radiotherapy and chemotherapy have limited role in the treatment of ameloblastic carcinomas. Close periodic reassessment of the patient is mandatory.

**Keywords** Ameloblastoma · Ameloblastic carcinoma · Odontogenic tumor

### Introduction

Ameloblastoma is a benign but locally aggressive odontogenic epithelial neoplasm, which presents as a slowly growing

painless swelling of the jaws. It constitutes about 1–3% of all jaw tumours and cysts [1]. It occurs more commonly in blacks than in whites [2]. The maxillomandibular ratio of ameloblastoma is 5:1 with more susceptibility in the mandible, and the most common site of occurrence is the mandibular molar region [3, 4]. More than 50% of recurrence occurs within the first 5 years after primary surgery [3].

Malignant variants of the ameloblastoma are exceptionally rare and may arise de novo or from transformation of a long-standing primarily benign lesion which has undergone several surgical excision [5]. Ameloblastic carcinoma (AC) is an extremely rare, aggressive malignant epithelial odontogenic tumor and has a poor prognosis. Two thirds of these tumors arise from the mandible while one third originates in the maxilla [6]. The most common symptom is a rapidly progressing painful swelling [7]. It may also present as a cystic lesion with benign clinical features or as a large tissue mass with ulceration, significant bone resorption and tooth mobility [8].

Terms malignant ameloblastoma and ameloblastic carcinoma have been used interchangeably for these variants in the past, it is now generally agreed that malignant ameloblastoma tends to metastasizes in spite of the benign histology in both the primary and the metastatic lesion [9, 10] while ameloblastic carcinoma exhibit histologic features of both ameloblastoma and carcinoma [9, 11]. The tumour may metastasize and histologic features of malignancy may be found in either the primary tumour, the metastases or both [7, 11].

More than 3600 cases of ameloblastomas have been described in the literature, [12] but less than 60 cases of ameloblastic carcinoma have been reported so far, among which two thirds occurred in the mandible [13].

Both aetiology of this rare carcinoma and the question whether this type of carcinoma originates from an ameloblastomas or represents a separate entity are still

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controversial [13]. There are difference of the opinion regarding treatment of ACs; however, wide surgical excision with or without radiotherapy is the most commonly used treatment modality [9].

### Case Report

A 21 year old male patient reported to the department of oral and maxillofacial surgery CSMMU Lucknow, with chief complaint of swelling over right side of face causing facial asymmetry, mild pain during mastication and difficulty in mouth opening, since last 3 months.

Patient was asymptomatic 6 months earlier he noticed a painless swelling over the right side of the face. He consulted a dentist, his mandibular right 2nd and 3rd molars were extracted. The patient realized the swelling grew in size even after the extraction of teeth. He reported to the department 3 months after that with a mild pain the same region. Patient belongs to middle class socioeconomically. He had no habit of smoking, and tobacco chewing (Fig. 1).

On examination a swelling was present over the right angle ramus region of mandible extending from preauricular area to mid of right cheek. The skin over swelling was normal in colour and texture. The swelling was mildly tender, hard in consistency, smooth, with ill defined margins.

Mouth opening was 46 mm with no deviation of mandible. Intraoral examination showed presence of all teeth except right mandibular 2nd and 3rd molars. Swelling was observed posterior to right 1st molar extending to the anterior border of ramus and coronoid process with



**Fig. 1** Preoperative photograph of the patient showing slight swelling at right side



**Fig. 2** Intra oral photograph



**Fig. 3** OPG showing radiolucency at right side

expansion of buccal and lingual cortical plates. Overlying mucosa was normal in colour, mildly tender and firm to hard in consistency (Fig. 2).

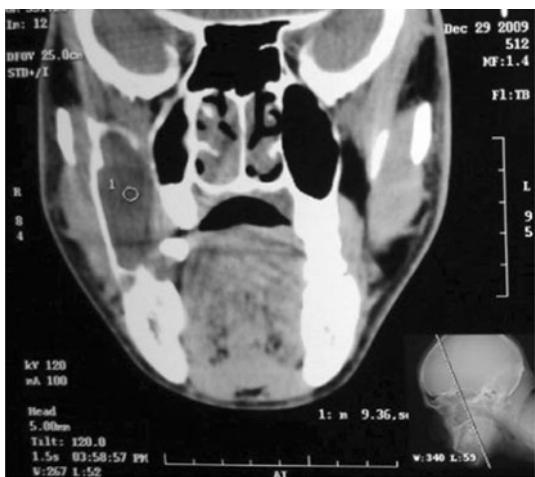
Radiological examination showed unilocular, radiolucent shadow with scalloped borders extending from mandibular right 2nd molar to coronoid process and involving the whole anteroposterior portion of ramus. CT scan showed, lesion involving right ramus and coronoid process of mandible measuring  $2.5 \times 4.5 \times 6.0$  cm in size, thinning of cortex and with cortical breach at multiple sites while right condyle was spared (Figs. 3, 4, and 5).

Incisional biopsy of the lesion was done and histological examination revealed nest of ameloblastic epithelium with surrounding myxoid stroma epithelium showing multi layering at places. The cells had increased nucleocytoplasmic ratio, hyper chromatic nuclei and were present in sheets. Focal areas of keratinization were also evident. Few mitotic figures were also present. Histomorphology was consistent of Ameloblastic Carcinoma with evidence of keratinization (Fig. 6).

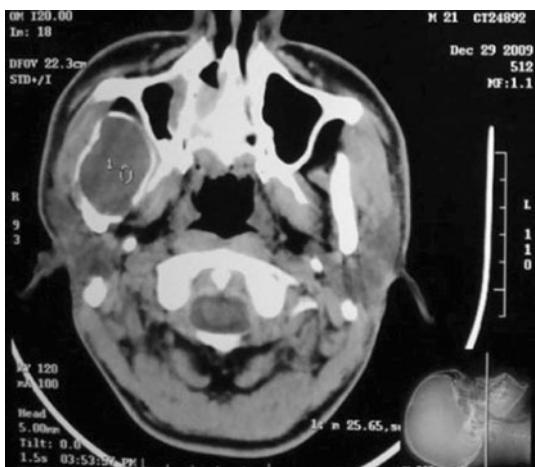
On the basis of biopsy segmental mandibulectomy (first premolar to ramus) was done taking safe margins of 1 cm. Chemotherapy and radiation was not advised. No metastases reported during the 2 year follow up period.

### Discussion

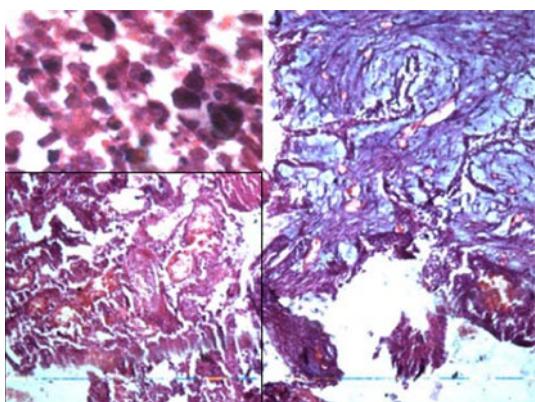
The ameloblastoma is an odontogenic tumour of the jaws, arising from dental embryonic remnants possibly from the



**Fig. 4** Computed tomogram coronal view



**Fig. 5** Computed tomogram axial view



**Fig. 6** Histopathology of the lesion, *inset* picture showing high magnification of the lesion

epithelial lining of an odontogenic cyst; dental lamina or enamel organ; stratified squamous epithelium of the oral cavity; or displaced epithelial remnants [8]. The malignant

form of ameloblastoma has been controversial for many years. The term ‘malignant ameloblastoma’ implies that lesions metastasize despite their benign histology. The term ameloblastic carcinoma (AC) is reserved for an ameloblastoma with a malignant morphologic appearance, regardless of the presence of metastasis [7].

ACs are extremely rare malignant odontogenic epithelial neoplasm and may arise de novo or from a pre-existing odontogenic lesion [9, 14]. They typically involve the mandible and less often the maxilla [7].

The embryological development of the sinonasal tract and the odontogenic apparatus are closely related to each other. The oral cavity and sinonasal tract communicate until the 10th intrauterine week [6]. These two cavities are separated by the development of the palatine shelves [16]. During this period, the odontogenic epithelium may be trapped in the sinonasal mucosa, or the sinonasal cells may acquire the capability of odontogenesis [16]. Odontogenic tumors may originate from the pluripotent cells of the basal layer of the oral and sinonasal epithelium [17, 18]. Ectopic teeth in the nasal cavity may also be a source for odontogenic neoplasm [15].

Ameloblastic carcinoma occurs in a wide range of age groups. There is no apparent sex predilection. The most commonly involved area is the posterior portion of the mandible [10]. Involvement of the maxilla by ameloblastic carcinoma seems to be less frequent than that of the mandible [9, 10]. The most common sign is swelling, although others include associated pain, rapid growth, trismus and dysphonia [10].

Radiological investigations include both the plain X-ray and computerized axial tomography. They appear as osteolytic processes, exhibiting a unilocular or multilocular appearance on radiograph. Screening for metastatic disease should be done, especially in recurrent cases of typical ameloblastoma, malignant ameloblastoma, and ameloblastic carcinoma [19].

Radiographic appearance of the AC is consistent with that of an ameloblastoma except for the presence of some focal radiopacities, apparently reflecting dystrophic calcifications. These histologic and radiologic features are not generally seen in conventional ameloblastomas.

Clinically, these carcinomas are more aggressive than typical ameloblastomas. Perforation of the cortical plate, extension into surrounding soft tissue, numerous recurrent lesions and metastasis, usually to cervical lymph nodes, can be associated with ameloblastic carcinomas [10].

The main differential diagnosis for this tumor was squamous cell carcinoma, in particular, the basaloid variant. In this case the features that distinguished the AC from squamous cell carcinoma included the jigsaw puzzle-type nesting of the tumor cells, the presence of stellate reticulum, and the distinctive cystic degeneration of the nests.

The diagnosis of craniopharyngioma can be also considered in the differential diagnosis, primarily because of its well known similarities to odontogenic neoplasia and partially because of its location in the cranial base. However, these possibilities are ruled out because the findings were characteristic of AC [7].

Surgical resection is the treatment of choice. En bloc removal with 1–2 cm of normal bone margin is the safest surgical modality to ensure disease-free survival. This method has resulted in local recurrence rates of less than 15% [19].

There is controversy regarding radiotherapy of Ameloblastoma, and it is considered radioresistant tumour [20]. There is no well-documented evidence concerning the true radioresponsiveness of these tumors. Authors have doubt on its effectiveness [21, 22]. But Atkinson et al. [23] retrospectively reviewed ten patients with ameloblastomas treated with megavoltage irradiation and concluded that ameloblastoma is not an inherently radioresistant tumor and that properly applied megavoltage irradiation has a useful role in the management. He also concluded that primary radiation should be considered whenever a full-surgical excision was technically difficult because of local invasion or inappropriate because of medical factors. Recommended treatment dosages are between 3,000 cGy and 5,000 cGy. Most of the ameloblastic carcinomas are intraosseous; therefore, the effectiveness of radiation therapy must be considered critically [13].

Chemotherapy as primary treatment does not appear indicated. Results of such treatment for non metastatic disease have been poor [24]. However, in the setting of metastatic disease, Ramadas et al. [25] found the use of cisplatin, adriamycin, and cyclophosphamide to be beneficial. Methotrexate and leucovorin has been also used [19].

In the case presented by us, there was no evidence of regional or distant metastasis but there was histological evidence of typical ameloblastic areas and foci with anaplastic cells in the same tumour. In addition, there was cellular pleomorphism and nuclear hyperchromatism with occasional mitoses in the same tumour.

Slootweg and Muller [9] and Daramola et.al [26] described a case of ameloblastoma which later exhibited cytological evidence of malignancy in the primary lesion after multiple surgeries suggesting that repeated trauma caused by surgery could be responsible for the malignant transformation.

Although we could not ascertain unequivocally whether ameloblastic carcinoma in our patient developed de novo or from a pre-existing ameloblastoma, we believe the former might be the most likely due to the absence of any history of previously operated tumour from the site and the short duration of the lesion.

Multiple local recurrences, repeated surgical procedures, and radiotherapy or chemotherapy frequently precede metastases from ameloblastoma [27]. Dissemination may result from increased malignant behaviour, stimulated by multiple recurrences or that the repeated surgical procedures required for the treatment of these recurrences, causes implantation of tumor cells into blood vessels or lymphatic channels. Laughlin [28] observed disease-free interval between the initial diagnosis and the appearance of metastases was 9 years. However, once metastases occurred, the median survival was 2 years.

ACs can recur locally 0.5–11 years after definitive therapy [29]. Distant metastasis is usually fatal and may appear as early as 4 months or as late as 12 years post-operatively [29]. The most common site for a distant metastasis is the lung, followed by bone, liver, and brain [2, 29]. Distant metastasis can occur in the absence of a local or regional recurrence [2].

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